REMARKS

FORMAL MATTERS:

Claims 26, 28-29, 54-60, 66-68, 70-75, and 80-86 are pending and currently under examination after entry of the amendments set forth herein.

Claims 26, 28-29, 54-60, 66-68, 70-75 and 80-86 were rejected.

Claim 71 is amended to even more clearly recite the present invention.

No new matter is added.

REJECTION UNDER 35 U.S.C. §103(a)

Claims 26, 28-29, 54-60, 66-68, 70-75, and 80-86 were rejected under 35 U.S.C. §103(a) as allegedly being obvious over Manning et al. (WO 97/38698) ("Manning") Applicants respectfully traverse the rejection as discussed below.

The Patent Office bears the burden of establishing a prima facie case of obviousness under 35 U.S.C. §103(a). *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). In order to meet its burden, the Office must first demonstrate that the prior art teaches or suggests all the claimed limitations. See, *Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007).

In addition, the Supreme Court in *KSR* emphasized that consideration of prior art that teaches away from the claimed invention is also relevant to the determination of obviousness. The Court stated that "when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007) (citing *United States v. Adams*, 383 U.S. 39, 40). See also, *Dystar Textilfarben GmbH v. C.H. Patrick Co.*, wherein the Federal Circuit stated that "[once] all claim limitations are found in a number of prior art references, the factfinder must determine '[w]hat the prior art teaches, whether it teaches away from the claimed invention, and whether it motivates a combination of teachings from different references.'" *Dystar Textilfarben GmbH v. C.H. Patrick Co.*, 464 80 U.S.P.Q.2d 1641, 1646 (Fed. Cir. 2006), *citing In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004).

Finally, as recognized by the Office in the MPEP §2143.01, "[i]f [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." The Federal Circuit stated a similar principle in *In re Gordon*, indicating that where the proposed modification would render the prior art invention unsatisfactory for its intended purpose, the prior art invention effectively teaches away from the proposed modification. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984)

As currently amended, Claim 71, the sole independent claim, recites:

A method for delivering a therapeutic agent into the inner ear of a living subject, said method comprising:

providing a drug delivery unit comprising a carrier material and a therapeutic agent combined therewith, wherein said carrier material provides for controlled release of the therapeutic agent from said drug delivery unit over time, and further wherein

said drug delivery unit is configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, or strand, and

said drug delivery unit is shaped and sized for partial or complete insertion into the round window niche of the subject; and

inserting said drug delivery unit directly into the round window niche of the subject such that said unit is positioned either partially or completely within the round window niche, wherein the therapeutic agent is released from the drug delivery unit, contacts the round window membrane and passes into the inner ear.

Applicants respectfully submit that Manning fails to teach or suggest at least the following elements of claim 71:

- ***"providing a drug delivery unit . . . wherein said drug delivery unit is configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, or strand".***
- ***"said drug delivery unit is shaped and sized for partial or complete insertion into the round window niche of the subject", and***
- ***"inserting said drug delivery unit directly into the round window niche of the subject such that said unit is positioned either partially or completely within the round window niche"***

First, Manning clearly fails to provide any teaching or suggestion with respect to a drug delivery unit "***configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, or strand***" as presently claimed. In fact, Manning's disclosure teaches away from a drug delivery unit having such a structure. This is because Manning teaches a fluid composition lacking a structure such that "**[t]he composition is fluid enough to be injected through a fine gauge needle (as small as 26 gauge).**" Manning at page 5, lines 24-25. See, also, Manning at page 10, lines 21-23, indicating that **"[t]he composition is always somewhat fluid, unlike solid implants or microspheres or other controlled release dosage forms**." This disclosure of Manning directs a person of ordinary skill in the art away from a drug delivery unit having a defined structure, such as those set forth in claim 71, in favor of a composition of such fluidity that the composition may be injected through a fine gauge needle. Manning teaches that such fluidity assures proper placement of the composition. See, Manning at page 5, line 25.

The Office proposes a modification of the composition of Manning which would result in Manning's fluid composition having one or more of the structures set forth in claim 71. However, Applicants submit that such a modification would render the composition of Manning **unsatisfactory for its intended purpose** because it would no longer be "fluid enough to be injected through a fine gauge needle" and accordingly Manning's goal of assuring proper placement via injection of a fluid composition would be thwarted. Thus, in accordance with the law as set forth in *In re Gordon*, **Manning effectively teaches away from the proposed modification**.

In the Final Office Action mailed April 18, 2011, the Office notes that "the list of structures in claim 70 [presumably claim 71 is meant] is taken from a list in the specification (see page 12) wherein the list in the specification also recites 'amorphous masses, gels, pastes, and the like.'" Final Office Action, pg. 6. The Office concludes that "[i]t is clear that the applicant did not see any patentable difference between the recited structures listed in the specification." *Id.* Finally, the Office states, without providing support of any kind, that "the recited structures are clearly design considerations and lack criticality" and "[t]he recited structures listed in the claims are well known and would be easily modified into the method of Manning."*Id.*

Applicants respectfully disagree with the conclusions drawn and the statements made by the Office in the above paragraph. There is simply no basis for the Office's conclusion that the Applicants

did not see a patentable difference between the items listed on page 12 of the specification. Furthermore, what Applicants may or may not have considered patentable at the time of drafting the application is irrelevant to the current analysis since applicants are entitled to prosecute claims which are narrower in scope than the original disclosure. Furthermore, the primary prior art reference cited by the Examiner contradicts the Office's statements that "the recited structures are clearly design considerations and lack criticality" and "[t]he recited structures listed in the claims are well known and would be easily modified into the method of Manning."

As discussed above, Manning explicitly directs a person of ordinary skill in the art away from a drug delivery unit having a defined structure, such as those set forth in claim 71. In addition, the Office's proposed modification of Manning which would result in Manning's fluid composition having one or more of the structures set forth in claim 71, would render the composition of Manning unsatisfactory for its intended purpose because it would no longer be "fluid enough to be injected through a fine gauge needle" and accordingly Manning teaches away from such a modification.

Second, the pending claims explicitly recite that "***said drug delivery unit is shaped and sized for partial or complete insertion into the round window niche of the subject***". There is simply no such teaching or suggestion in Manning. Specifically, the only description provided by Manning with respect to the structure of its dosage form is a characterization of the dosage form as a fluid, which lacks a defined structure, such that it is capable of being injected through a fine gauge needle. Accordingly, Manning fails to teach or suggest a drug delivery unit **shaped and sized** for partial or complete insertion into the round window niche of the subject.

In response, the Office argues that "[t]he composition of Manning has a substantial viscosity and therefore has a shape and size. The composition is delivered to the round window niche and will always have a size and shape and therefore meets the limitations." Final Office Action, page 7.

Applicants respectfully disagree with the above conclusion of the Office. The claims require not only that the drug delivery unit has a shape and a size, but that the drug delivery unit is "shaped and sized" **for partial or complete insertion into the round window niche of the subject**. Thus, the instant claims require a defined structure, i.e., a pellet, disk, tablet, plate, sphere, cube, cylindrical unit,

or strand, and require further that such pellet, disk, tablet, plate, sphere, cube, cylindrical unit, or strand is shaped and sized for partial or complete insertion into the round window niche of the subject. Such a drug delivery unit is simply not taught or suggested by Manning which clearly teaches a fluid composition having none of the above recited structures.

Third, Manning fails to teach or suggest "***inserting said drug delivery unit directly into the round window niche of the subject such that said unit is positioned either partially or completely within the round window niche.***" Manning merely discloses injection or pumping of its fluid dosage form "behind the ear drum" to the middle ear. See, e.g., Manning at page 5, lines 20-23. While such injection may result in some amount of the dosage form eventually reaching the round window niche, it does not amount to a teaching or suggestion to insert a drug delivery unit as explicitly claimed in the instant application, i.e., ***directly into the round window niche of the subject***. As discussed in the instant specification, placement of the drug delivery unit directly into the round window niche can provide several advantages over a more generalized delivery, e.g., avoiding premature drug delivery and inadvertent delivery to other tissue regions outside the round window niche. See, e.g., page 21, line 32 – page 22, line 4 of the instant application as filed.

In response, the Office points to the disclosure of Manning on page 4, lines 10-14, wherein Manning recites that "upon insertion into the middle ear, the composition is capable of maintaining its position in order to provide a surface that substantially contacts the round window membrane of the middle ear and providing extended release of active agent to the inner ear." However, the cited section of Manning is describing the positioning of the composition **following insertion**. It does not describe the insertion process or insertion location itself. Instead, Manning's insertion location is described broadly as the middle ear behind the ear drum. As this encompasses a large area relative to the round window niche, there is simply no teaching or suggestion in Manning to insert **directly** into the round window niche.

With specific reference to claim 70, Applicants note that the Office has failed to demonstrate that Manning teaches or suggests a method as claimed in claim 71, which includes the additional limitation of claim 70, "***wherein release of the therapeutic agent from the drug delivery unit is without inadvertent delivery to other tissue regions outside the round window niche***." As discussed above,

Manning teaches injection or pumping of a fluid dosage form "behind the ear drum" to the middle ear. If anything, the teachings of Manning suggest that inadvertent delivery to tissue regions outside the round window niche would be likely because of the fluid nature of the dosage form and the fact that Manning does not teach inserting a drug delivery unit directly into the round window niche of the subject. Accordingly, Manning neither teaches nor suggests a method "***wherein release of the therapeutic agent from the drug delivery unit is without inadvertent delivery to other tissue regions outside the round window niche***."

With specific reference to claims 83 and 85, Applicants note that the Office has failed to demonstrate that Manning teaches or suggests a method as claimed in claim 71, which includes the additional limitation of claim 83 ***"wherein said drug delivery unit is shaped and sized for complete insertion into the round window niche of the subject***" or claim 85 ***"wherein said drug delivery unit is shaped and sized for complete insertion as a detached unit into the round window niche of the subject"***. At most, Manning teaches insertion into the middle ear such that the composition contacts the round window membrane, however, there is no teaching or suggestion in Manning that the composition is shaped and sized for complete insertion into the round window niche of the subject.

With specific reference to claim 86, Applicants note that the Office has failed to demonstrate that Manning teaches or suggests a method as claimed in claim 71, which includes the additional limitation of claim 86 ***"wherein said drug delivery unit is positioned at a location which is spaced apart from the round window membrane."*** In fact, Manning teaches the opposite. Manning explicitly teaches that its composition is in contact with the round window membrane. See, e.g., Manning at page 3, lines 26-29; and page 4, lines 10-14.

In view of the above, Applicants submit that the Office has failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103(a) over Manning. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 72-74 were rejected under 35 U.S.C. §103(a) as allegedly being obvious over Manning in view of Peterson (U.S. Patent No. 4,472,394) "Peterson". Applicants respectfully traverse the rejection as discussed below.

According to the Office, Manning teaches the invention substantially as claimed. The Office relies on Peterson solely for an alleged teaching of extended release of an active agent over a period of 60 days to 210 days. Office Action, page 5. The specific deficiencies in the Manning disclosure with respect to the claimed invention are set forth above. As Peterson's alleged teaching of extended release of an active agent over a period of 60 days to 210 days in no way cures the specific deficiencies present in Manning, the proposed combination of references fails to establish a *prima facie* case of obviousness for claims 72-74 which incorporate each of the limitations of independent claim 71.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0185, order number DURE-021.

Respectfully submitted,
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